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Zealand plays catch-up with Shire in short bowel syndrome

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Shire made a big bet on short bowel syndrome with last year's acquisition of NPS Pharma and its lead product, Gattex, a GLP-2 agonist that is still the only drug approved for the disorder.

But competition is on the horizon in the form of Zealand Pharma's ZP1848, which has just started phase II development, putting it ahead of several other mainly preclinical GLP-2-targeting candidates (see table below). Crucially, ZP1848 has a couple of advantages that might help it grab market share from Shire – and, in a rare disease like short bowel syndrome, every patient counts.

The approval of Gattex in 2012 was a major step forward in the disorder as it helped reduce the need for intravenous feeding, a mainstay of therapy that is expensive and linked with complications including infections and liver and kidney problems.

Room for improvement

But Gattex is still "far from the perfect drug", Bryan Garnier analysts wrote. They believe that ZP1848 could have better efficacy, helped by its longer half-life of 14-17 hours, versus less than two hours for Gattex.

ZP1848 also promises greater convenience – both are injected subcutaneously but Zealand's is given via a ready-to-use pen, while Gattex requires a multistep reconstitution process before being delivered by a syringe.

It should not be too long until we get the first hints of whether ZP1848 is indeed more effective, with results from the 18-patient phase II study due next year. Zealand hopes to show a reduction from baseline in faecal wet weight output, an indication of improvement in intestinal absorption.

It is still too early for most analysts to have included Zealand's project in their expectations, but a couple have made forecasts: Bryan Garnier expects unadjusted peak sales of $1.75bn in 2026, and a probability of success of 30%; while Goldman Sachs sees risk-adjusted peak sales of $250m, based on a 45% chance of approval.

GLP-2 number two

And, while ZP1848 is Zealand's most advanced short bowel syndrome candidate, it has another GLP-2 agonist slightly ahead on the development path, but in chemotherapy-induced diarrhoea. Phase IIb data with elsiglutide, which is licensed to Helsinn, are expected in the second half of this year.

Selected GLP-2 agonists in development

Agent	Company	Status	Indication
Gattex	Shire/NPS	Marketed	Short bowel syndrome
ZP1848	Zealand Pharma	Phase II	Short bowel syndrome
Elsiglutide	Zealand Pharma/Helsinn	Phase II	Chemotherapy-induced diarrhoea
MDGN-205	Medgenics	Preclinical	Short bowel syndrome
NB1002	Naia Pharmaceuticals/ Amunix	Preclinical	Short bowel syndrome

Short bowel syndrome is often caused by surgical resection of the small intestine, owing to cancer or Crohn's disease, for example. Symptoms and severity vary, but patients can have a reduced ability to absorb water and nutrients from their diet.

GLP-2 agonists aim to reduce the incidence of diarrhoea and the need for intravenous nutrition by slowing gastric emptying, reducing inflammation and promoting regeneration of the epithelial surface of the gut.

The market, at least by patient numbers, is fairly small – *EP Vantage* has previously estimated 2,000-6,000 potential users (*Natpara risk overshadows Shire's NPS takeout, January 12, 2015*).

But with Gattex priced at around $300,000 per patient per year, this is still a large opportunity. Under NPS, the drug brought in $32m in 2013, but with Shire's marketing power revenues could reach $579m by 2020, according to *EvaluatePharma* consensus.

And Shire's muscle could make it difficult for Zealand to carve out a niche for ZP1848 – making it even more important that the next-gen GLP-2 shows signs of better efficacy in phase II.

Project	Study	No. of patients	Primary endpoint	Results due	ID
ZP1848	Phase II proof-of-concept trial in short bowel syndrome	18	Change from baseline in faecal wet weight output	2017	Not available
Elsiglutide	Phase IIb trial in chemotherapy-induced diarrhoea	600	Proportion of patients experiencing Grade ≥2 diarrhoea	H2 2016	NCT02383810

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